

REMARKS

Upon entry of the amendments presented herein, claims 1, 2, 4, 5, 6, 8, 11, 13, 35, and 36 are pending in the instant application. New claims 35 and 36 have been added. Claims 1, 2, 4, 5, 6, 8, 11, and 13 have been amended. Claims 3, 7, 9, 10, 12, 14 and 15 have been cancelled, while claims 16-34 have been withdrawn. Support for the amendments to claims 1, 4, 5, 6, 8, 11, and 13 can be found throughout the specification as filed and in original claims 2 and 10. Applicant has amended the specification to include a Related Applications section. No new matter has been added by the amendments herein.

Objections to the Specification

The Examiner has objected to the specification because of the use of improperly demarcated trademarks. *See*, Office Action at page 4. Applicant has amended the specification herein to properly demarcate trademarks used therein. This objection should be withdrawn.

The Examiner has objected to claims 7 and 9 for failing to provide antecedent basis for the claims. *See*, Office Action at page 5. Claims 7 and 9 have been canceled, thus this objection is moot and should be withdrawn.

Claim Rejections -- 35 U.S.C. § 101

Claims 1-9, 11 and 13 are rejected under 35 U.S.C. § 101, because the claimed invention is directed to non-statutory subject matter. *See*, Office Action at page 5. Applicant has amended independent claims 1 and 13 to require that the claimed animal is a mouse. Accordingly, claims 1-9, 11 and 13 are drawn to statutory subject matter. This rejection should be withdrawn.

Claim Rejections -- 35 U.S.C. § 112

Claims 7-9 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. *See*, Office Action at page 6. Claims 7 and 9 have been canceled. Thus, this rejection is moot as it applies to these claims. Claim 8 has been amended to require that the cell is isolated “from”

said mouse. Accordingly, Applicants assert that claim 8 is definite. This rejection should be withdrawn.

Claims 1, 6-10 and 13-15 are rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement. *See*, Office Action at page 7. Independent claims 1 and 13 have been amended to include the limitation of claim 3, which the Examiner has acknowledged meets the written description requirement. As such, Applicant asserts the claims as amended satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. This rejection should be withdrawn.

Claims 1-9, 11, and 13-14 are rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement. *See*, Office Action at page 12. Independent claims 1 and 13 have been amended to require that the mammal is a mouse, for which the Examiner has acknowledged meets the enablement requirement. As such, Applicant asserts the claims as amended satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. This rejection should be withdrawn.

Claim Rejections -- 35 U.S.C. § 102

Claims 1-2, 7-11, and 13-15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Muller *et al.* (Mol. Cell Bio 20(9):3316-3329, 2000; “Muller”). *See*, Office Action at page 17.

According to the Examiner, Muller teaches a transgenic mammal comprising a recombinant nucleic acid stable integrated into the genome of said mammal, said recombinant nucleic acid comprising a cyclin A1 promoter operably linked to a nucleic acid. *See*, Office Action at page 17. Claim 1, has been amended to incorporate the limitations of claim 3, which the Examiner has acknowledged is novel in view of Muller. This rejection should be withdrawn.

Claims 1-4, 6-8, 10-11, and 13-15 are rejected under 35 U.S.C. § 102(e) as being anticipated by Holland (US Patent No. 7,041,869; “Holland”) as evidenced by Genebank Accession AF516106.1, GI:2136179. *See*, Office Action at page 18.

According to the Examiner, Holland teaches a transgenic mouse comprising an E2F1-promoter operably linked to luciferase. Applicant has submitted herewith a declaration under 37

C.F.R. § 1.131 demonstrating that the invention was made prior to the earliest priority date of Holland. Accordingly, Applicant asserts that Holland is not prior art under 35 U.S.C. § 102(e).

New claims 35 and 36 require that the promoter is a dihydrofolate reductase promoter, a DNA polymerase alpha promoter, a c-myc promoter, or a B-myb promoter. Applicants assert that Holland does not teach the specifically recited promoters required by new claims 35 and 36, and therefore Holland does not anticipate the invention as claimed.

Claim Rejections -- 35 U.S.C. § 103

Claims 3-7 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Muller in view of Neuman *et al.* (Mol. Cell Bio. 14(10):6607-6615, 1994; “Neuman”), Hsiao *et al.* (Genes & Development 8:1526-1537, 1994; “Hsiao”) and Jaenisch (Science 240:1468-1474, 1998; “Jaenisch”) as evidenced by Muller *et al.* (J. Biol. Chem. 274 (16):11220-11228, 1999; “Muller II”) and Di Lella *et al.* (N.A.R. 16(9):4149, 1998; “DiLella”). *See*, Office Action at page 20. Claims 3, 7, and 12 have been canceled. As such, this rejection, as it applies to these claims, is moot and should be withdrawn.

Applicants traverse the rejection of claims 4-6 on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness. A *prima facie* case of obviousness requires that “either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references.” *See* MPEP 706.02(j) citing *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). Knowledge of the disclosure provided by the instant application must be put aside when determining whether the claimed invention would have been obvious. *See* MPEP 2142.

To support the conclusion that the claimed invention is directed to obvious subject matter, the Examiner has cited and combined up to six references. The mere fact that these references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one ordinary skill in the art. *See* MPEP §2143.01, citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007). Furthermore, a statement that modifications of the prior art to meet the claimed invention would have been “well within the ordinary skill of the art at the time the claimed invention was made” because the references relied upon teach that all aspects of the claimed invention were

individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *See* MPEP §2143.01, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (emphasis original).

There is no objective reason provided by the Muller, Neuman, Hsiao, Jaenisch, Muller II and DiLella references, alone or in combination, that would lead the skilled artisan to combine and/or modify these references, nor is there any evidence that the resultant combination of these references would have been predictable. These references fail to provide the skilled artisan with a reasonable expectation that the mouse recited by claims 4-6 could be produced.

Muller (as acknowledged by the Examiner) does not teach or suggest a transgenic mouse having a recombinant nucleic acid molecule stably integrated into the genome of the mouse, wherein the recombinant nucleic acid molecule comprising an E2F responsive promoter is operably linked to a nucleic acid encoding a bioluminescent protein. Neuman, Hsiao, Jaenisch, Muller II and DiLella each fail to cure the deficiencies in the teachings of Muller.

Neuman and Hsiao merely describe a specific E2F1 promoter having a specific sequence. Nothing in either Neuman or Hsiao teaches or suggests the specifically recited mouse of claim 1. Jaenisch, Muller II and DiLella each fails to remedy the deficiencies in the teachings of Muller, Neuman, and Hsiao, as each fails to describe the specifically recited mouse of claim 1.

As such, there is no objective reason provided in any of the cited references, alone or in combination, which would lead the skilled artisan to arrive at the claimed invention. Moreover, there is no evidence that the results generated by combining and/or modifying these references would have been predictable at the time the instant invention was made. Any suggestion that it would have been obvious to replace the promoter taught by Muller, Neuman, and Hsiao, is an improper application of hindsight based on Applicants' disclosure in the instant application. Thus, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness and request that this rejection be withdrawn.

CONCLUSION

Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

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